

(19) World Intellectual Property Organization
International Bureau

INTERNATIONAL PATENT CLASSIFICATION: A61K 48/00

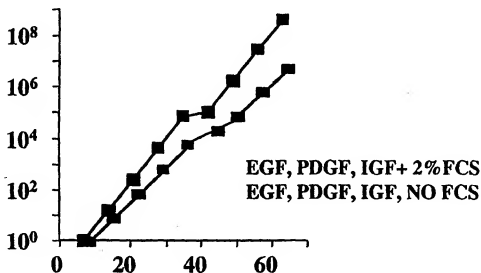
(43) International Publication Date
15 February 2001 (15.02.2001)

PCT

(10) International Publication Number
WO 01/11011 A3

- (51) International Patent Classification⁷: C12N 5/06, A61P 35/00, A61K 48/00
- (21) International Application Number: PCT/US00/21387
- (22) International Filing Date: 4 August 2000 (04.08.2000)
- (25) Filing Language: English
- (26) Publication Language: English
- (30) Priority Data:
60/147,324 5 August 1999 (05.08.1999) US
60/164,650 10 November 1999 (10.11.1999) US
- (71) Applicants and
(72) Inventors: FURCHT, Leo, T. [US/US]; 2100 West 21st Street, Minneapolis, MN 55405 (US). VERFAILLIE, Catherine, M. [BE/US]; 585 Cretin Avenue South, St. Paul, MN 55116 (US). REYES, Morayma [US/US]; 1011 29th Avenue S.E., Apartment C, Minneapolis, MN 55414 (US).
- (74) Agent: VIKSNINS, Ann, S.; Schwegman, Lundberg, Woessner & Klueh, P.O. Box 2938, Minneapolis, MN 55402 (US).
- (84) Designated States (*national*): AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW.
- (84) Designated States (*regional*): ARIPO patent (GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG).
- Published:
— With international search report.
- (88) Date of publication of the international search report: 10 May 2001
- For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

(54) Title: MULTIPOTENT ADULT STEM CELLS AND METHODS FOR ISOLATION



(57) Abstract: The invention provides isolated stem cells of non-embryonic origin that can be maintained in culture in the undifferentiated state or differentiated to form cells of multiple tissue types. Also provided are methods of isolation and culture, as well as therapeutic uses for the isolated cells.

INTERNATIONAL SEARCH REPORT

Int'l Application No

PCT/US 00/21387

A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 C12N5/06 A61P35/00 A61K48/00

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 C12N A61K A61P

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, WPI Data, PAJ, BIOSIS, MEDLINE, SCISEARCH, CHEM ABS Data, EMBASE, BIOTECHNOLOGY ABS

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 95 10599 A (BRANDON MALCOLM ROY ; WILLIAMS ROBERT LINDSAY (AU); UNIV MELBOURNE) 20 April 1995 (1995-04-20) page 12; table 1	1-3, 8-30, 50-60
X	ROSFJORD EDWARD ET AL: "The octamer motif present in the Rex-1 promoter binds Oct-1 and Oct-3 expressed by EC cells and ES cells." BIOCHEMICAL AND BIOPHYSICAL RESEARCH COMMUNICATIONS, vol. 203, no. 3, 1994, pages 1795-1802, XP000979460 ISSN: 0006-291X	1-3
A	page 1797, last paragraph -page 1798, paragraph 1; figure 1B --- -/-	6

☒ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

* Special categories of cited documents:

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search

6 February 2001

Date of mailing of the international search report

21/02/2001

Name and mailing address of the ISA
European Patent Office, P.B. 5816 Patentlaan 2
NL - 2280 HV Rijswijk
Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,
Fax: (+31-70) 340-3016

Authorized officer

ALCONADA RODRIG., A

INTERNATIONAL SEARCH REPORT

Int'l Application No
PCT/US 00/21387

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	HILTON D J ET AL: "DISTRIBUTION AND COMPARISON OF RECEPTORS FOR LEUKEMIA INHIBITORY FACTOR ON MURINE HEMOPOIETIC AND HEPATIC CELLS" JOURNAL OF CELLULAR PHYSIOLOGY, vol. 146, no. 2, 1991, pages 207-215, XP000981564 ISSN: 0021-9541	7-17, 20-30, 50-60,62
Y	figures 1,4,6; tables 1,3	18
X	ROSNER M H ET AL: "OCT-3 IS A MATERNAL FACTOR REQUIRED FOR THE FIRST MOUSE EMBRYONIC DIVISION" CELL, vol. 64, no. 6, 1991, pages 1103-1110, XP000979417 ISSN: 0092-8674 page 1104, left-hand column, last paragraph -page 1105, right-hand column, paragraph 1; figure 2	31
X	WO 95 03062 A (CELLPRO INC) 2 February 1995 (1995-02-02) claims 1,2	32,33, 46,48
Y	page 8, line 6-14	34,35
X	CA 2 191 655 A (STEMCELL TECHNOLOGIES INC) 2 June 1997 (1997-06-02) page 6, line 16-30 page 19, line 6 -page 23, line 31	32,33,46
Y		34,35
Y	CASSIEDE PIERRE ET AL: "Osteochondrogenic potential of marrow mesenchymal progenitor cells exposed to TGF-beta-1 or PDGF-BB as assayed in vivo and in vitro." JOURNAL OF BONE AND MINERAL RESEARCH, vol. 11, no. 9, 1996, pages 1264-1273, XP000981538 ISSN: 0884-0431 figures 2,3; tables 1,2	34
X	US 5 635 386 A (ARMSTRONG R DOUGLAS ET AL) 3 June 1997 (1997-06-03) column 8, line 7-18 column 13, second table see OTHER COMPONENTS column 9, line 8-24	36,38-44
Y		35,37,45
X	WO 99 35243 A (BEACH DAVID H ;WANG JING (US); COLD SPRING HARBOR LAB (US); HANNON) 15 July 1999 (1999-07-15) claims 1-4,14-18	47
	--- -/--	

INTERNATIONAL SEARCH REPORT

Int lional Application No

PCT/US 00/21387

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT		
Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	EP 0 627 487 A (IMMUNEX CORP) 7 December 1994 (1994-12-07)	49
Y	page 4, line 11-20 page 5, line 57,58	18
Y	LENNON DONALD P ET AL: "A chemically defined medium supports in vitro proliferation and maintains the osteochondral potential of rat marrow-derived mesenchymal stem cells." EXPERIMENTAL CELL RESEARCH, vol. 219, no. 1, 1995, pages 211-222, XP000981537 ISSN: 0014-4827 the whole document	37
Y	WO 99 11758 A (CARPENTER MELISSA; CYTOTHERAPEUTICS INC (US)) 11 March 1999 (1999-03-11) page 5, line 5-8 page 5, line 21 -page 6, line 9 page 9, line 19-29 example 1	45
A	PITTENGER M F ET AL: "MULTILINEAGE POTENTIAL OF ADULT HUMAN MESENCHYMAL STEM CELLS" SCIENCE, US, AMERICAN ASSOCIATION FOR THE ADVANCEMENT OF SCIENCE,, vol. 284, no. 5411, 2 April 1999 (1999-04-02), pages 143-147, XP000867221 ISSN: 0036-8075 cited in the application the whole document	1-5
A	BEN-SHUSHAN ETTI ET AL: "Rex1, a gene encoding a transcription factor expressed in the early embryo, is regulated via Oct-3/4 and Oct-6 binding to and octamer site and a novel protein, Rox-1, binding to an adjacent site." MOLECULAR AND CELLULAR BIOLOGY, vol. 18, no. 4, April 1998 (1998-04), pages 1866-1878, XP002159568 ISSN: 0270-7306 page 1868, right-hand column, paragraph 2; figure 2 abstract	6

INTERNATIONAL SEARCH REPORT

Int. Patent Application No.
PCT/US 00/21387

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	RAPTIS A ET AL: "Polymorphism in CD33 and CD34 genes: A source of minor histocompatibility antigens on haemopoietic progenitor cells?" BRITISH JOURNAL OF HAEMATOLOGY, vol. 102, no. 5, 1998, pages 1354-1358, XP000981540 ISSN: 0007-1048 the whole document	61
A	WO 99 27076 A (LORING JEANNE F ;ARC GENOMIC RESEARCH (US)) 3 June 1999 (1999-06-03) page 20, line 4-16	63

INTERNATIONAL SEARCH REPORT

Information on patent family members

Int. Application No.

PCT/US 00/21387

Patent document cited in search report		Publication date		Patent family member(s)		Publication date
WO 9510599	A	20-04-1995	AU	7934594 A	A	04-05-1995
WO 9503062	A	02-02-1995	AU	7404494 A	A	20-02-1995
CA 2191655	A	02-06-1997		NONE		
US 5635386	A	03-06-1997	US	5399493 A		21-03-1995
			AU	3422893 A		28-07-1993
			WO	9312805 A		08-07-1993
			AU	687674 B		26-02-1998
			AU	5059296 A		11-07-1996
			AU	665525 B		11-01-1996
			AU	9175091 A		22-07-1992
			CA	2100268 A		18-06-1992
			EP	0575350 A		29-12-1993
			JP	11221074 A		17-08-1999
			JP	6505151 T		16-06-1994
			JP	2000189157 A		11-07-2000
			KR	225307 B		15-10-1999
			WO	9211355 A		09-07-1992
			US	5670351 A		23-09-1997
			US	5437994 A		01-08-1995
			US	5670147 A		23-09-1997
			US	5646043 A		08-07-1997
			US	5605822 A		25-02-1997
			AT	148502 T		15-02-1997
			CA	2062741 A		16-12-1990
			DE	69029856 D		13-03-1997
			DE	69029856 T		04-09-1997
			DK	477290 T		21-07-1997
			EP	0477290 A		01-04-1992
			EP	0753574 A		15-01-1997
			ES	2097149 T		01-04-1997
			JP	4506153 T		29-10-1992
			KR	196062 B		15-06-1999
			KR	201662 B		15-06-1999
			KR	201663 B		15-06-1999
			WO	9015877 A		27-12-1990
			US	5459069 A		17-10-1995
			US	5763266 A		09-06-1998
			US	5888807 A		30-03-1999
WO 9935243	A	15-07-1999	AU	2317299 A		26-07-1999
			EP	1045697 A		25-10-2000
EP 0627487	A	07-12-1994	US	5554512 A		10-09-1996
			AU	683472 B		13-11-1997
			AU	6987794 A		20-12-1994
			BR	9407073 A		27-08-1996
			CA	2162397 A		08-12-1994
			CN	1125479 A		26-06-1996
			CZ	9503079 A		16-10-1996
			FI	955646 A		23-01-1996
			HU	74831 A		28-02-1997
			JP	8511251 T		26-11-1996
			NO	954735 A		23-01-1996
			NZ	267541 A		24-06-1997
			PL	311756 A		18-03-1996

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/US 00/21387

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
EP 0627487 A		WO 9428391 A	08-12-1994
		US 5843423 A	01-12-1998
		ZA 9403490 A	23-01-1995
		AU 702179 B	18-02-1999
		AU 2098295 A	25-09-1995
		CN 1142247 A	05-02-1997
		EP 0749472 A	27-12-1996
		FI 963373 A	29-08-1996
		NO 963630 A	07-11-1996
		NZ 282999 A	19-12-1997
		WO 9524469 A	14-09-1995
WO 9911758 A	11-03-1999	US 5968829 A	19-10-1999
		AU 9305998 A	22-03-1999
		EP 1007636 A	14-06-2000
		US 6103530 A	15-08-2000
WO 9927076 A	03-06-1999	AU 1704899 A	15-06-1999
		EP 1060244 A	20-12-2000